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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/582,410	09/19/2006	Per Holm	Lp-31011-US	4705

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EXAMINER	
PAGONAKIS, ANNA	
ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
02/04/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/582,410	HOLM ET AL.	
	Examiner	Art Unit	
	ANNA PAGONAKIS	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 November 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-48* is/are pending in the application.

4a) Of the above claim(s) *11,12,19-23,32-35 and 47* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10, 13-18, 24-31, 36-46 and 48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2 sheets, 11/18/2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election of atorvastatin and the HMG-CoA inhibitor, 2-amino-2-(hydroxymethyl)-1,3-propanedoil as the stabilizer in the reply filed on 11/12/2008 is acknowledged. A search of the prior art found that the species for the disorders are co-extensive and therefore the disorder specie election set forth in the office action mailed on 7/28/2008 is withdrawn. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 1-48 are pending in the application. Claims 11-12, 19-23, 32-35 and 47 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected subject matter, there being no allowable generic or linking claim. Accordingly, no claims have been amended, cancelled or newly added.

This application is the national stage entry of PCT/DK06/50004 filed 2/10/2006; and claims benefit of foreign priority document DENMARK PA 2005 00200 filed 2/10/2005 and further claims benefit of foreign priority document DENMARK PA 2005 00576 filed 4/20/2005.

Claims 1-10, 13-18, 24-31, 36-46 and 48 are currently under examination and the subject of this Office Action.

Objection

Claim 1 is objected to because of the following informalities: claim 1 is missing an article "a" before "second solid composition". Appropriate correction is required.

Claims 29, 30 and 48 are objected to because of the following informalities: claims 29 and 30 recite a composition which comprises a "solid solution." There is no such thing as solid solution. The composition is either a solid or a solution/liquid. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 29 and 30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 29 and 30 recites the limitation "the active substance". There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-10, 13-16, 27-31, 36, 38-46 and 48 are rejected under 35 U.S.C. 102(b) as being anticipated by Guivarc'h et al (U.S. 6,534,808).

Guivarc'h et al teach of an orally administered pharmaceutical composition for the treatment of elevated levels of cholesterol and related conditions comprising a statin and fenofibrate in the form of microparticles of a solid fenofibrate that are stabilized by phospholipid as a surface active substance (abstract). Formulations prepared can be dried into powders, optionally blended with excipients or bulking agents, and then can be filled into capsules or converted into granules or tablets with the addition of binders and other excipients known in the art of table making (column 45). The dosage form can be a tablet preferably a coated tablet with moisture resistant or moisture retardant layer, additionally with an enteric coating (column 46). The amount of fenofibrate per capsule or tablet can range from about 20 mg to about 300 mg, and preferably from about 40 mg to about 300 mg and is most preferably 40 mg to 50

mg, 51 mg, 52 mg, 53 mg, 54 mg, 67 mg, 100 mg, 102 mg, 103 mg, 104 mg, 134 mg, 150 mg, 153 mg, 156 mg, 159 mg, 160 mg, 200 mg, 213 mg, 250 mg and 300 mg of fenofibrate per capsule or tablet (column 46). Preferred statins include atorvastatin in a range between 2 mg to 100 mg (column 39). Micronized fenofibrate and fenofibrate compositions were prepared in the presence of starch (Figure 1). Among the excipients included were lactose and mannitol (claim 41). Microcrystalline cellulose can be used as an excipient in tablet formation of atorvastatin (column 3). Guivarc'h et al teach that the microparticalse of fenofirbrate can comprise a number of possible compositions (see column 43, lines 37-52) including mixture of fenofibrate and statin in different particles, regions of fenofibrate and statin phase separated in the same particle (column 40 lines 7-17).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-10, 13-16, 24-31, 36, 38-46 and 48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Guivarc'h et al (U.S. 6,534,088) in view of Cink et al (U.S. 2005/0148594), as evidenced by MeSH Descriptor Data, 2007 .

Guivarc'h et al teach of an orally administered pharmaceutical composition for the treatment of elevated levels of cholesterol and related conditions comprising a statin and fenofibrate in the form of microparticles of a solid fenofibrate that are stabilized by phospholipid as a surface active substance (abstract). Formulations prepared can be dried into powders, optionally blended with excipients or bulking agents, and then can be filled into capsules or converted into granules or tablets with the addition of binders and other excipients known in the art of table making (column 45). The dosage form can be a tablet preferably a coated tablet with moisture resistant or moisture retardant layer, additionally with an enteric coating (column 46). The amount of fenofibrate per capsule or tablet can range from about 20 mg to about 300 mg, and preferably from about 40 mg to about 300 mg and is most preferably 40 mg to 50 mg, 51 mg, 52 mg, 53 mg, 54 mg, 67 mg, 100 mg, 102 mg, 103 mg, 104 mg, 134 mg, 150 mg, 153 mg, 156 mg, 159 mg, 160 mg, 200 mg, 213 mg, 250 mg and 300 mg of fenofibrate per capsule or tablet (column 46). Preferred statins include atorvastatin in a range between 2 mg to 100 mg (column 39). Micronized fenofibrate and fenofibrate compositions were prepared in the presence of starch (Figure 1). Among the excipients included were lactose and mannitol (claim 41). Microcrystalline cellulose can be used as an excipient in tablet formation of atorvastatin (column 3).

Cink et al teach of fenofibrate and tromethamine where the fenofibric acid content may comprise other active substances such as atorvastatin (paragraph [0039]). MeSH teaches that 2-amino-2-(hydroxymethyl)-1,3-propanediol is also named tromethamine. Clink et al teach that these salt forms can be used to treat hyperlipidemia or coronary heart diseases (paragraph [0004]). An object Cink et al to provide pharmaceutical formulations that make fenofibric acid sufficiently bioavailable and prevent

recrystallization of the active substance, i.e. atorvastatin (paragraph [0010]). Enteric binders include polyethylene glycol 6000 (paragraph [0054]).

In view of the teachings of the cited prior art, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to administer the formulation of Guivarc'h et al in combination with the formulation of Cink et al. Such motivation arises from the fact that both references teach improved oral formulations of fenofibrate and atorvastatin. Guivarc'h teaches this improved formulation with additional excipients including lactose, mannitol and microcrystalline cellulose and enteric coatings. Cink et al teach tromethamine and polyethylene glycol 600 in the formulation which provides increased bioavailability. Therefore, it would have been obvious to one of ordinary skill in the art to administer the excipients and coatings of the formulations of Guivarc'h et al with those of Cink et al in order to achieve the present formulation with a reasonable expectation that the combination would render an improved oral and bioavailable composition.

Claims 17-18 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Guivarc'h et al (U.S. 6534,088) in view of Cink et al (U.S. 2005/0148594), as evidenced by MeSH Descriptor Data, 2007, as applied to claims 1-10, 13-16, 24-31, 36, 38-46 above, and further in view of Ohsawa et al (U.S. 2004/0023919).

The combination of Guivarc'h et al (U.S. 6534,088) in view of Cink et al (U.S. 2005/0148594), as evidenced by MeSH Descriptor Data, 2007 is set forth *supra*. The combination differs by not comprising the administration of an antioxidant.

Ohsawa et al teaches that HMG-COA reductase inhibitor, such as atorvastatin, with ascorbic acid derivatives reduces total cholesterol levels (paragraph [0005] and claim 2).

One of ordinary skill in the art would have found it prima facie obvious to administering atorvastatin with ascorbic acid and the claimed formulations of Guivarc'h et al and Cink et al, since as

disclosed ascorbic acid leads to reduction in cholesterol. Such a person would have been motivated to do so in order to improve the efficacy of treatment of atorvastatin and thus, the suggestion to make such a combination flows logically from the very fact that each was known in the prior art to have the same therapeutic utility and, in turn, raises the reasonable expectation of success that the two therapies when combined have, at minimum, additive effects.

With respect to claims 17-18, the determination of the optimum pH of the claimed solid dosage form would also have been a matter well within the purview of the skilled artisan. Such a determination would also have been made in accordance with a variety of factors, such as modifying the pharmaceutical carriers used to formulate the dosage form to optimize palatability of the dosage form and to maximize tolerability of the composition. In addition, the skilled artisan would also have been motivated to optimize the pH of the solution in order to maintain the active pharmaceutical ingredients in their desired salt form without any degradation of the active ingredients that may occur due to a change in pH.

Conclusion

No claim is found to be allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANNA PAGONAKIS whose telephone number is (571)270-3505. The examiner can normally be reached on Monday thru Thursday, 9am to 5pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

AP

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614